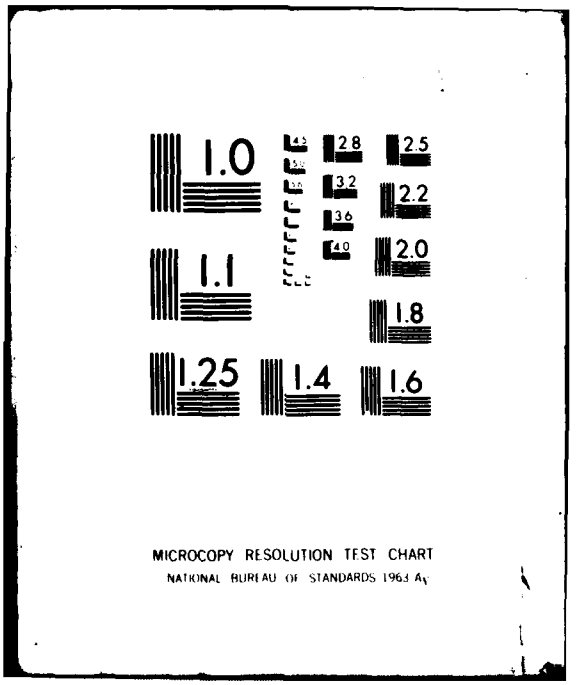
AD-A107 302 OFFICE OF NAVAL RESEARCH LONDON (ENGLAND) F/G 6/5
INTERNATIONAL SYMPOSIUM ON NUCLEAR TECHNIQUES IN THE STUDY AND --ETC(U)
SEP 81 H STEK
UNCLASSIFIED ONRL-C-7-81 NL


1.0
1.1
1.25
1.4
1.6
1.8
2.0
2.2
2.5
2.8
3.2
3.6
4.0
MICROCOPY RESOLUTION TEST CHART
NATIONAL BUREAU OF STANDARDS 1963 A

LEVEL II

AD A107302

ONR LONDON CONFERENCE REPORT

C-7-81

OFFICE OF NAVAL RESEARCH

BRANCH OFFICE LONDON ENGLAND

INTERNATIONAL SYMPOSIUM ON NUCLEAR TECHNIQUES IN THE STUDY AND CONTROL OF PARASITIC DISEASES OF MAN AND ANIMALS

MICHAEL STEK, JR*

1 SEPTEMBER 1981

* Uniformed Services University, Bethesda, MD

UNITED STATES OF AMERICA

UNCLASSIFIED

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

REPORT DOCUMENTATION PAGE

READ INSTRUCTIONS BEFORE COMPLETING FORM

1. REPORT NUMBER: ONRL-C-7-81	2. GOVT ACCESSION NO.: AD-A107 302
3. RECIPIENT'S CATALOG NUMBER:	
4. TITLE (and Subtitle): INTERNATIONAL SYMPOSIUM ON NUCLEAR TECHNIQUES IN THE STUDY AND CONTROL OF PARASITIC DISEASES OF MAN AND ANIMALS.	5. TYPE OF REPORT & PERIOD COVERED: Conference Report,
	6. PERFORMING ORG. REPORT NUMBER: C-7-81
7. AUTHOR(s): MICHAEL STEK, JR	8. CONTRACT OR GRANT NUMBER(s):
9. PERFORMING ORGANIZATION NAME AND ADDRESS: OFFICE OF NAVAL RESEARCH BRANCH OFFICE LONDON BOX 39 FPO NY 09510	10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS:
11. CONTROLLING OFFICE NAME AND ADDRESS:	12. REPORT DATE: 1 September 1981
	13. NUMBER OF PAGES: 4 / 256
14. MONITORING AGENCY NAME & ADDRESS (if different from Controlling Office):	15. SECURITY CLASS. (of this report): UNCLASSIFIED
	15a. DECLASSIFICATION/DOWNGRADING SCHEDULE:

16. DISTRIBUTION STATEMENT (of this Report)

APPROVED FOR PUBLIC RELEASE: DISTRIBUTION UNLIMITED

Accession For
NTIS GRA&I X
DTIC TAB
Unannounced
Justification
By
Distribution/
Availability Codes
Dist Special
A

17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)

18. SUPPLEMENTARY NOTES

19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

antigen assays
antiparasitic vaccines
chemotherapeutic agents
immunoassays

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

This is a report of a meeting at which ideas were exchanged on the application of nuclear techniques and the the use of radioisotopes in the research and development of serodiagnostic and seroepidemiological procedures, antiparasitic vaccines, and chemotherapeutic agents. Techniques which the author judged to have special significance are discussed.

265000

DD FORM 1 JAN 73 1473 EDITION OF 1 NOV 65 IS OBSOLETE
S/N 0102-LF-014-6601

UNCLASSIFIED

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

INTERNATIONAL SYMPOSIUM ON NUCLEAR TECHNIQUES IN THE STUDY AND CONTROL OF PARASITIC DISEASES OF MAN AND ANIMALS

The International Symposium on Nuclear Techniques in the Study and Control of Parasitic Diseases of Man and Animals was held at the International Atomic Energy Agency in Vienna, Austria, on 29 June through 3 July, 1981. Participants from 36 nations attended. The purpose of the symposium was to bring together scientists from the developed and developing countries for the exchange of ideas on the application of nuclear techniques and the use of radioisotopes in the research and development of serodiagnostic and seroepidemiologic procedures, antiparasitic vaccines, and chemotherapeutic agents. The symposium specifically recognized advances in this field including improved radioimmunoassays, successful immunization in animal models against protozoan and helminthic disease, and identification and purification of antigens employing radiolabelling techniques.

Radioimmunoassays

Radioimmunoassays (RIAs) and related procedures such as enzyme-immunoassays (EIAs), have been developed to high levels of sensitivity. The functional RIAs that are presently available for the major parasitic diseases of man, including amebiasis, toxoplasmosis, malaria, leishmaniasis, schistosomiasis, and filariasis, were discussed at the symposium. Of note was a paper by J. P. Dessaint and A. Capron (Centre d'Immunologie et de Biologie Parasitaire, Inst. Pasteur, Lille Cedex, France) entitled "Nuclear Techniques in Seroepidemiology and Diagnosis of Parasitic Diseases," in which they reported on the development of assays to detect circulating antigens as well as antibodies. Until recently, serodiagnostic procedures for the parasitic diseases have relied on antibody detection. The antibody schemes, although sensitive, have been plagued with relative lack of specificity. The antigen assays appear more specific and offer quantitative analyses which will aid investigators to explore the humoral response more fully.

J. Golenser, H. Avraham, D. T. Spira, and D. Sulitzeanu (Hebrew Univ. Hadassah Medical School, Jerusalem), presented a paper entitled "Practical Applications of a Solid-Phase RIA of *Plasomodium falciparum* Antigens and Anti-plasmodial Antibodies." Schizont extracts, prepared from washed, and then disrupted, infected red cells, were used as antigens bound to plastic in a solid-phase system. The antibodies in patients' sera were identified by iodine-radiolabelled staphylococcus protein A. Sera from patients parasitologically positive produced high binding of protein A, while sera from parasitologically negative patients yielded significantly lower degrees of binding. The antigen assay was conducted as an inhibition assay. Patients' erythrocytes containing the suspected antigens internally or on their surface were washed and then mixed with a known amount of high-titered anti-*P-falciparum* antibody, and this was reacted with the antigen-coated plastic tubes. The erythrocyte-associated antigen levels were estimated as inversely proportional to

the degree of radiolabelled protein A binding. This assay offers a specific and sensitive (able to detect as little as $1/10^7$ organisms in the peripheral blood) serologic tool. Although promising, this test appears too cumbersome for true field applicability.

A paper by M. Nuti, R. D'Amelio, R. Seminara, L. Palmisano, and F. Aiuti (Rome Univ., Italy) entitled "Circulating Immune Complexes Detected by Clq Solid Phase Assay in Amebiasis" attempted to focus on a concept currently in vogue in immunobiology, that of immune complex associated diseases. Clq was used in this study to capture circulating immune complexes (CIC). However, since the procedure probed the antibody portion of the moeity with polyvalent antihuman antisera, the CIC detected may not necessarily be parasite related. The results were quite interesting, nonetheless. Italian cyst passers and infected Africans demonstrated significantly higher CIC levels than were observed in unmatched Italian or African controls. The African control sera gave higher values than Italian controls. The assumption was that this association might be due to the fact that Africans have greater numbers of infectious disease problems, but this was not documented. The authors also stated that "CIC can display a pathogenetic role in clinical manifestations of amebiasis." The data presented did not include immunopathology and therefore would not support such a conclusion.

Radiation Attenuated Vaccines for Protozoan Infections

Effective vaccines employing irradiated parasites have been produced for a number of protozoan systems including the sporozoites of *Plasmodia*, blood forms of *Babesia*, tachyzoites of *Toxoplasma* and the trypanosomes in animal models. The most substantial progress has been made with the *Plasmodia*. Two papers reported success with the use of irradiation-attenuated blood stages of *Plasmodium berghei* in rodents. The first, by M. Yadav, S. D. Sekaram, and J. S. Dhaliwal (Univ. of Malaya, Kuala Lumpur, Malaysia), was entitled "Induction of Protection in Rats and Mice with Radiation-Attenuated *Plasmodium berghei*." The second was written by S. Boonpucknavig, V. Boonpucknavig, and S. Viriyakosul (Mahidol Univ., Bangkok, Thailand) and had the title "Immunological and Pathological Consequences in Mice Vaccinated with Radiation Attenuated Blood Stages of *Plasmodium berghei*." Both studies employed infected red blood cells which were irradiated with gamma irradiation and injected IP (*intra peritoneally*) as a vaccine. Both reported significant reductions in the immunized groups when compared to the controls. This blood stage approach might alleviate a major problem with the irradiated sporozoite vaccine. While the sporozoite vaccine has been shown to establish immunity, the supply of sufficient organisms for large-scale vaccine production has been lacking. The *in vitro* production of blood stage parasites could be a practical solution to this supply problem.

In specific regard to the sporozoite vaccine, a paper by J. M. Ramsey, M. R. Hollingdale, and R. L. Beaudoin (Naval Medical Research Inst., Bethesda, MD; and the Biomedical Research Inst., Rockville, MD)

entitled "The Infection of Tissue Culture Cells with ^{60}Cobalt Irradiated Malaria Sporozoites" demonstrated that irradiated sporozoites could be induced to enter cells in culture and remained normal through at least the early exoerythrocytic stages. This suggests, as the authors concluded, that in actual vaccine use, the irradiated sporozoites penetrate cells *in vivo*.

Radiation Attenuated Vaccines for Helminthic Infections

Promising vaccines have been prepared against schistosomes with irradiated cercariae and schistosomula in various host systems, i.e., rodents and cattle. Furthermore, in primate studies immunity has been induced against the three major human species. Encouraging results reported at the symposium by M. Stek, M. A. Stirewalt, F. Lewis, and V. Schinski (Uniformed Services Univ., Biological Research Inst., and the Naval Medical Research Inst., Bethesda, MD) in a paper entitled "Immunization of Cynomolgus Monkeys with Cryopreserved Irradiation Attenuated *Schistosoma mansoni* Schistosomula" support the efficacy of the radiation-attenuated vaccine approach. Also, the success of the cryopreserved vaccine offers the opportunity to stockpile doses and contemplate vaccine production. It should be noted that the efficacy of this vaccine was not dependent on total immunity. Reduction of the worm burden reduced the egg load and thus the degree of clinical presentation.

Radiated vaccines have also been developed for *Ancylostoma caninum* in dogs, *Dictyoculus viviparus* in cattle, and *Brugia malayi* in monkeys.

For the radiation attenuated vaccines in general, conference attendees agreed that the technical aspects of vaccine production required standardization. Further, a clear understanding of the mechanism of immunogenecity, as augmented by irradiated parasites, has yet to be established. Analysis methods as reported by S. M. Phillips and W. A. Ried (Univ. of Pennsylvania School of Medicine, Philadelphia), in a paper entitled "The use of Radiobiologic Technology in Schistosomiasis," focused on *in vitro* radiolabelling of cercariae which then were traced in the host by means of that label. This paper dealt with the interaction dynamics between the rat host and the schistosome parasite which supported the conclusion that the surface membrane and the host's specific response are critical in parasite elimination.

Similar work has been done in the malaria mouse model with isotopic labelling of sporozoites by R. L. Beaudoin, R. J. Moon, R. A. Vrable, and N. D. Pacheco (Naval Medical Research Inst., Bethesda, MD, and Michigan State Univ., East Lansing). Their paper, entitled "Distribution of ^{51}Chromium Labelled Sporozoites of *Plasmodium berghei* in Naive and Immune Mice" supported studies which suggested that irradiated sporozoites enter cells and transform into exoerythrocytic forms. In addition, it demonstrated that challenge infective sporozoites are retained by the liver in the immunized and nonimmunized animals.

Isotopic labelled parasites offer a powerful tool to probe the localization of parasites in the host and the mechanisms of induced immunity.

Radiolabelling Techniques in Probing Parasite Antigens

Identification and isolation of specific parasite antigens are essential for the purification of immunogens which could potentially be employed as "killed" vaccines and as immunodiagnostic tools for clinical and epidemiological studies. Sensitive radioisotopic methods for protein antigen analysis were presented by C. A. P. Tavares, M. N. Cordeiro, and G. Gazzinelli (Centro de Pesquisas Rene Rachou, Minas Gerais, Brazil) in a paper entitled "Identification and Characterization of the Tegumental Surface Proteins of *Schistosoma mansoni*." These workers, employing autoradiographic patterns of young schistosomula and adult worms, were able to identify at least one stage-specific antigen for each stage.

In addition to the endogenous and exogenous labelling which must be accomplished to identify and localize parasite-derived proteins, carbohydrate and lipid moieties must also be assessed, particularly because they may contribute to antigenicity of the parasite and immunity in the host.

END

DATE
FILMED

12-81

DTIC